

Aus dem Pathologischen Institut der Universität Basel

(Vorsteher: Prof. Dr. A. Werthemann)

Arbeit unter Leitung von Prof. Dr. S. Scheidegger

Arteriovenous Angiomas of the Brain

A Report of two Cases with Autopsy

INAUGURAL-DISSERTATION

zur Erlangung der Doktorwürde
der Medizinischen Fakultät der Universität Basel

vorgelegt von

SEYMOUR A. LIEBOWITZ

von New York, New York

VERLAG P. G. KELLER - WINTERTHUR 1965

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Tag der Promotion: 29.6.1965



Vascular tumors of the Central Nervous System are uncommon neoplasms comprising approximately 2 % of all intracranial neoplasms. The terminology of these tumors is unusually difficult because widely different names are used to describe the same pathological picture.

In this work I shall adhere to the classification originally set forth by Cushing and Bailey, dividing these tumors into two main groups:

- I. Vascular malformations.
 1. Telangiectasis (a group of capillaries).
 2. Angioma venosum (lesions composed principally of veins).
 3. Angioma arteriale (lesions containing vessels resembling arteries as well as veins, i. e. arteriovenous angioma).
- II. Hemangioblastoma (angioblastoma).
 1. Cystic type (associated with cyst formation).
 2. Solid type (not associated with cyst formation).

Each of these two types is again classified into capillary, cellular and cavernous varieties according to the microscopic features.

The purpose of this paper is to present two cases of arteriovenous angiomas and to discuss the etiology and pathological anatomy of these tumors. I shall also discuss the problem of hemorrhage of these tumors.

It should be noted that clinical symptomatology and diagnosis will not be discussed in this work. For this, the reader is referred to the standard works of neurology.

CASE NUMBER ONE

Anamnesis

S. H. a 24 year old primipara in her 36th week of gestation, was admitted to the surgical clinic of the Basle University Hospitals, (Director, Prof. R. Nissen, M. D.), because of a sudden onset of headache, vomiting, and unconsciousness. The pregnancy up to this time was unremarkable. The patient was controlled regularly at the Women's Hospital of Basle, (Director, Prof. T. Koller, M. D.), and no signs of preeclampsia were noted.

Physical examination on admission revealed a comatose patient with marked nuchal rigidity. Kernig and Brudzinski signs were positive; the

pupils were miotic and did not react to light; Babinski responses were present bilaterally. BP was 145/75, Temperature 37,2° C. Lumbar-puncture yielded grossly bloody cerebrospinal fluid. A diagnosis of a ruptured aneurysm was made. Because the foetus was still viable, a caesarian section was performed. The child was delivered in good condition. The patient tolerated the procedure well, however, she died three hours post-operatively.

Post mortem S. N. 1112/63

There were signs of a central death; fluidity of the blood; mild peripheral emphysema of the lungs; the right ventricle of the heart was somewhat dilated. The myocard appeared oligemic and showed cloudy swelling. The kidneys and spleen showed passive hyperemia. The right kidney and ureter were larger than the left, however, the parenchyma of both kidneys were grossly normal. The liver showed a severe degree of passive hyperemia.

A Uterus puerperalis with a 6 cm. long fresh caesarian section incision was found. A typical gravid hypophysis and a corpus luteum of pregnancy in the left ovary were found.

After removing the calvarium the brain was seen to bulge forth; it appeared congested and swollen. The cerebellum was pressed into the foramen magnum. The pons was somewhat flattened. Hemorrhages were seen mainly in the area of the pons, cerebellum and medulla. Blood coagula were also noted in these areas. The arteries supplying the brain had a somewhat delicate structure. The left vertebral artery was hypoplastic, the right vertebral artery hyperplastic. No other vascular anomalies of the cerebral arteries were grossly noted.

The brain was fixed in formalin before being dissected.

On dissection, the fourth ventricle, aqueduct of the midbrain and both lateral ventricles were noted to be filled with blood coagula. Blood was also found in the large subarachnoid cisterns at the base of the brain. In the region of the right corpus striatum there was a sharply defined tumor measuring 20,5 mm. in diameter. Blood vessels could be seen on the surface of the tumor. These varied greatly in calibre and thickness. When the tumor was cut, they bulged forth. The tumor bordered on the internal capsule and right lateral ventricle. Blood coagula were found in all the ventricles of the brain. There were no signs of previous hemorrhage or cyst formation. The remainder of the brain revealed no other abnormalities on dissection.

Histology

Microscopically, the vessels of the tumor appeared tortuous and of varying calibre and thickness. On hematoxylin-eosin stain the veins appeared to outnumber the arteries, however, when stained for elastic tissue, a definite tunica elastica interna could be seen in many vessels. This led to the conclusion that the arteries outnumbered the veins. In many vessels no such distinction could be made. The intima of almost all vessels was thickened and hyalinized. In a small number of vessels this intimal proliferation almost obliterated the lumen of the vessel. In some vessels the endothelial cells were swollen and numerous.

Many vessels did not have a true tunica elastica interna but showed numerous elastic fibers running concentrically in the intima giving the impression of a true elastic membrane. (Process of arteriolization).

A definite muscular layer was present in many vessels. In some, this layer was clearly hypertrophied.

There appeared to be proliferation of the adventitia of many vessels. There was patchy calcium incrustations in some vessel walls, however, no thrombi, old or new, were noted.

The interstitial tissue surrounding the vessels was primarily a glial tissue with a mild inflammatory reaction. The adjacent brain tissue showed a moderate degree of encephalomalacia.

Microscopically, the kidney showed passive hyperemia. The glomerula were large with an abundance of cells. The tubules showed some cloudy swelling.

Resume of findings

An arteriovenous angioma of the right corpus striatum with hemorrhage into the right lateral ventricle was found. The tumor was composed of arteries and veins with proliferative changes in the vessel walls. The tissue surrounding the tumor showed glial reaction, encephalomalacia and some inflammation. The lumina of the vertebral arteries were unequal.

Careful and complete autopsy failed to show any other vascular abnormalities.

CASE NUMBER TWO

Anamnesis

E. G. an 84 year old female was admitted to the medical clinic of the Basle University Hospitals, (Director, Prof. F. Koller, M.D.), because of a heart arrhythmia. This did not respond to treatment with digitalis and procainamide. The patient developed an atrio-ventricular block and died 24 hours after admission. There was no history of neurologic disease and neurological examination on admission was within normal limits.

Post mortem S. N. 143/64

There was left and right ventricular dilatation of the heart. The myocardium was brown and atrophic. There was a bilateral hydrothorax and a moderate degree of arteriosclerosis of the peripheral vasculature.

The cerebral arteries showed no gross anatomical abnormalities.

The brain appeared grossly normal. It was then sectioned in the frontal plane, each slice measuring 2 cm. in thickness.

In the region of the mamillary bodies, beneath the thalamus, a brown, very soft area, about the size of a hazelnut, was noted. Within this somewhat cystic mass, a vascular tumor was noted. The remainder of the cerebrum, inclusive of the cerebellum and ventricles showed no abnormalities.

Histology

Microscopically, a few large cystic areas were noted. These cysts were lined by an endothelium. The tissue adjacent to the outside of the endothelium was a connective tissue composed of glial cells, fibroblasts and some capillaries.

Within some of the cysts a vascular tumor was noted. The latter was composed of both arterial and venous elements.

In one section of the tumor there appeared a conglomeration of vascular channels, most of which were filled with blood. These were composed, for the most part, of connective tissue walls. An endothelium and differentiated vessel walls were rarely seen. Evidence of old thrombosis was present. Hemorrhage around the vessels was also present.

Calcification of these vessels was moderate. Hemosiderin and inflammatory cells were a prominent part of this section of tumor.

In an adjacent cystic area, tortuous vessels of primarily arterial nature were found. The intima of these vessels was greatly thickened and hyalinized. The muscular layer was significantly hypertrophied. The adventitia appeared to be increased in size. Calcification of these vessels was patchy and minimal.

No normal brain tissue could be found adjacent to the tumor. Hemosiderin and macrophages were numerous. Areas of "fat granule cells", (microglia), circumscribed by a loose connective tissue were seen. There was a severe degree of encephalomalacia and gliosis.

Histological examination of other areas of the brain revealed no other abnormalities.

Resume of findings

An arteriovenous angioma of the regio subthalamica was found as an incidental autopsy finding. There was evidence of old bleeding and thrombosis within the tumor. Degenerative changes were parominent part of the tumor. The adjacent brain tissue showed a severe degree of encephalomalacia and gliosis with calcification.

DISCUSSION

In both tumors, the presence of arteries and veins with brain tissue in the interstitium has led to the diagnosis of arteriovenous angioma. There is no agreement today, among pathologists, as to the classification of these tumors. *Noran* has extensively reviewed the literature and cited no less than twelve different classifications of these tumors and added one of his own. The most widely accepted classification is based on the presence or absence of nerve tissue in the interstitium; the true tumors containing reticulin fibers and being devoid of nervous tissue in the interstitium of the tumor.

A prodigious amount of discussion has been recorded as to whether or not the tumors called angiomas are true neoplasms or mere malformations. *Cushing and Bailey, Raney and Courville, Levine, Luschka, Dandy and Russel and Rubenstein* are among those who expressed belief that these tumors represent congenital anomalies.

Bergstrand states that attempts to classify these lesions as either tumors or malformations are bound to be misleading as the two exceptions

do not exclude one another. He further states: "Most, perhaps all of the true hemangiomas are malformations which have attained autonomous growth." *Turner and Kernohan* agree in part with *Bergstrand* stating that the neoplastic growth may have had its' origin in the confines of a malformation. They stress, however, that the mode of progression of angiomas is through enlargement of the individual vessels and not by actual growth.

Arieti and Gray feel that no sharp distinction can be made between vascular neoplasms and vascular malformations of the brain.

Bergstrand, nevertheless, classifies angiomas as true neoplasms since it is often a space occupying lesion. *Schwartz*, *Virchow*, *Rippert*, *Simmonds* and *Heine* also expressed the opinion that angioma is a true neoplasm.

When one considers *Ewing's* definition of a neoplasm, as an uncontrolled new growth of tissue, it becomes clear, I believe, that the two terms should be kept separate as in almost all cases they represent separate entities.

The true tumors or angioblastomas (Hemangioblastomas) as *Cushing and Bailey* have named them, have been termed by a multitude of names. Among them: Gliosarcoma, endothelial sarcoma, perithelial sarcoma, angioendothelioma, angioblastic sarcoma, hemangioendothelioma, angio-reticuloma and capillary hemangioma.

Cushing and Bailey's term was originated because they felt this neoplasm closely resembled the various stages that the vessels in the chick embryo passthrough during their development, and theirs' is by far the most widely accepted term.

These tumors are primarily situated as solitary lesions in the cerebellum and are of varying size, sometimes quite large and generally well circumscribed and cystic. Grossly, they are massive, spongy, and of a reddish yellowish color.

Histologically, the vessels are tortuous, interwoven and may show dilatations. The cells are pleomorphic with a vesicular nucleus and often a nucleolus. In many places the richness of small cells gives the tumor the appearance of a sarcoma. At other times the cytoplasm is extensively filled with vacuoles giving the cell a foamy appearance, hence term "pseudoxanthomatosis". Mitotic figures are seldom seen.

A dense reticulum permeating the tumor is characteristic. The reticulum fibers encircle the capillaries and vascular spaces sending branches into the cellular intervascular areas.

To understand the possible etiology of arteriovenous malformations of the brain, one must briefly review *Streeter's* five stages of development of the vessels of the Central Nervous System:

- (1) Development of a primordial vascular network.
- (2) Differentiation of these vessels into arteries veins and capillaries.
- (3) Separation of the vessels with the dura, pia and arachnoid layers of the brain.
- (4) Branching of the vessels along with the brain as the latter develops.
- (5) Histological development of the vessels becomes complete.

During the second stage, an arteriovenous communication can occur if no capillary system is developed. These vessels will in time dilate and their walls will become altered. Such an arteriovenous communication can be found in any area of the brain.

During the third stage, a communication may arise between the middle meningeal artery and the subarachnoid veins.

Thus, a multitude of hypothetical possibilities, have been set forth to explain these communications.

Houdart and Le Besnerais feel that no satisfactory determinant for these malformations have, as yet, been set forth. Familial cases are very rare.

This brings us to those cases of vascular anomalies in which hereditary factors play a role, i. e. von Hippel-Lindau Disease and Osler's disease. Sturge-Weber-Dimitri Disease is considered congenital but not hereditary.

The characteristic feature of these diseases is the presence of vascular tumors in the brain and in other parts of the body. The individual gross and histological features of these vascular tumors does not vary with those occurring alone and therefore shall not be discussed in this work.

The problem of hemorrhage of the vascular tumors is by far the most important to the clinician. *Houdart and Le Besnerais* have reported that up to 75 % of these tumors present clinically with hemorrhage. Definitive histological changes which would explain such hemorrhages were absent in most cases.

Most authors feel, and I agree, that as the vessels enlarge, their walls undergo degenerative changes. The latter correspond to those of the formation of an arterial aneurysm where a weakness in the vessel wall gives rise to a bulging, often pulsating mass. If such a vessel reaches the surface of the brain or a ventricle, massive hemorrhage will occur. This was apparently the situation in our first case.

Bleeding within the tumor is not uncommon. It would appear, according to our second case, to be directly related to arteriosclerotic changes in the vessel walls.

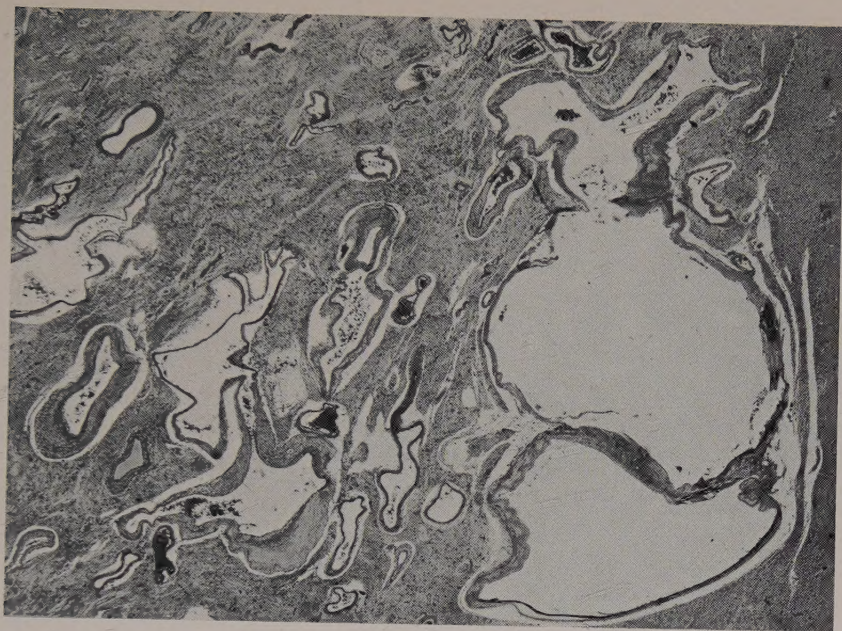
It is my hope that through a better understanding of the pathological picture of these tumors, the clinician and the surgeon will be better equipped to predict the course and prognosis of these lesions.

SUMMARY

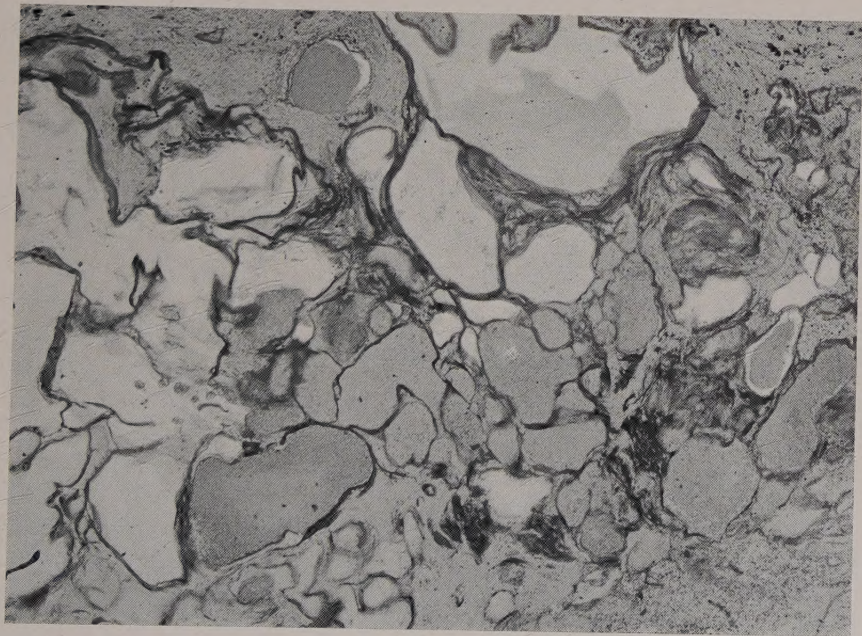
- (1) Two cases of arteriovenous angiomas with autopsy are described.
- (2) The classification of vascular tumors of the central nervous system is discussed.
- (3) The etiology of these tumors is discussed.
- (4) Hemorrhages of these tumors are discussed.

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Angiovenous Angioma of the Brain
Case 1. S. N. 1112/63 x 20



Angiovenous Angioma of the Brain
Case 2. S. N. 193/64 x 34

